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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/658,873	KOPRESKI, MICHAEL S.	
	Examiner	Art Unit	
	Frank W. Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *3,7,10,11,19,21,22,30,33-38,49 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6,8,9,12-18,20,23-29,31,32 and 39-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-34 and 39-50 and species (1) (the amplified product is produced from a tumor related RNA or cDNA produced therefrom, claims 4 and 8) and species (4) (the defined group or population comprises humans or animals with cancer, claims 12-16 and 23-27) in the reply filed on May 31, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). After reviewing claims 31, 32, 47, and 48, the examiner decides to withdraw species election on claims 31, and 32. Therefore, claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 39-48 will be examined.

Specification

2. The disclosure is objected to because of the following informality: since US application 10/013,868 now is US Patent No. 6,939,671, applicant is required to update this information in the first sentence of the specification.

Appropriate correction is required.

Claim Objections

3. Claims 40, 41, 43, and 44 are objected to because of the following informality: "A method" should be "The method".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Scope of enablement

Claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting a product amplified from total extracellular RNA from plasma or serum of a human or a animal, does not reasonably provide enablement for detecting, inferring, or monitoring any kind of disease such as any kind of cancer or premalignancy in a human or animal using the methods recited in claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 45, and 46 and evaluating a human or animal for any kind of disease such as any kind of cancer or premalignancy using the methods recited in claims 31, 32, 47, and 48. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the

breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to show that the methods recited in claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 45, and 46 can be used for detecting, inferring, or monitoring any kind of disease in a human or animal and the methods recited in 31, 32, 47, and 48 can be used for evaluating a human or animal for any kind of disease such as any kind of cancer or premalignancy. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability how the methods recited in claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 45, and 46 can be used for detecting, inferring, or monitoring any kind of disease such as any kind of cancer or premalignancy in a human or animal and the methods recited in claims 31, 32, 47, and 48 can be used for evaluating a human or animal for any kind of disease such as any kind of cancer or premalignancy.

Claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 45, and 46 are directed to a method for detecting, inferring, or monitoring any kind of disease such as any kind of cancer or premalignancy in a human or animal while claims 31, 32, 47, and 48 are directed to a method for evaluating a human or animal for any kind of disease such as any kind of cancer or premalignancy. The specification only shows that tyrosinase cDNA amplified from total RNA of serum of patients with malignant melanoma can be used for identifying a patient either having melanoma or having a high risk for melanoma (see pages 24 and 25). However, the specification does not provide a guidance to show that the methods recited in claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 45, and 46 can be used for detecting, inferring, or monitoring any kind of disease such as any kind of cancer or premalignancy in a human or animal and the methods recited in claims 31, 32, 47, and 48 can be

used for evaluating a human or animal for any kind of disease such as any kind of cancer or premalignancy. First, since the claims do not limit to a specific disease such as a specific cancer and do not limit to a specific gene and there is no evidence to show that any kind of gene correlated to any kind of disease can be detected from serum or plasma or any kind of bodily fluid, it is unclear how to detect, infer, or monitor any kind of disease such as any kind of cancer or premalignancy in a human or animal using the methods recited in claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 45, and 46 and how to evaluate a human or animal for any kind of disease such as any kind of cancer or premalignancy using the methods recited in claims 31, 32, 47, and 48. Second, since the specification does not show to perform the methods recited in claims 5, 6, 8, 20, 23-29, 32, and 48 by amplifying total RNA from a non-cellular fraction of any kind of bodily fluid from a human or animal wherein bodily fluid from a human or animal can be urine, sputum, vomitus, gastro-intestinal contents, cerebrospinal fluids, saliva, milk, pertioneal fluid, embryonic fluid, vaginal or cervical secretions and semen and there is no evidence to show that any kind of gene correlated to any kind of disease can be detected from any kind of bodily fluid, it is unclear how to detect, infer, or monitor any kind of disease such as any kind of cancer or premalignancy in a human or animal using the methods recited in claims 5, 6, 8, 20, and 23-29 and how to evaluate a human or animal for any kind of disease such as any kind of cancer or premalignancy using the methods recited in claims 32 and 48.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether the methods recited in claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 45, and 46 can be used for

detecting, inferring, or monitoring any kind of disease such as any kind of cancer or premalignancy in a human or animal and the methods recited in claims 31, 32, 47, and 48 can be used for evaluating a human or animal for any kind of disease such as any kind of cancer or premalignancy.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 9, 12-20, 23-29, 31, 32, 39-44, 47, and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 9 or 20 is rejected as vague and indefinite. Since the claim does not limit that a defined group or population is from a human or animal, it is unclear how to detect, infer or monitor a disease in a human or animal by comparing the amount or concentration or comparative value of total extracellular RNA or one or a plurality of an RNA species to a reference range RNA amount, concentration, or value determined from a species which is not a human or animal. Furthermore, although claim 9 or 20 is directed to a method to detect, infer or monitor a disease in a human or animal, the claim does not indicate how value of total extracellular RNA or one or a plurality of an RNA species is correlated to a disease as recited in claims 1 and 5. Please clarify.

9. Claim 31 or 32 is rejected as vague and indefinite. Although claim 31 or 32 is directed to a method of evaluating a human or animal for a disease, there is no method step for evaluating a human or animal for a disease and the goal of the claim cannot be reached. Please clarify.

10. Claims 39 and 42 are rejected as vague and indefinite. Since total extracellular RNA or one or a plurality of RNA species thereof in the claims is not labeled or labeled with a compound that can generate a color, it is unclear how to comparing signal intensity, color intensity, and color of total extracellular RNA or one or a plurality of RNA species thereof. Furthermore, since claims 39 and 42 do not indicate that a reference group or population is from a human or animal or not. If a reference group or population is not from a human or animal, it is unclear how to perform the methods recited in claims 39 and 42 by comparing an amount or concentration of total extracellular RNA or one or a plurality of RNA species using blood serum or plasma or bodily fluid from different species. Please clarify.

11. Claims 41 and 44 are rejected as vague and indefinite because electrochemiluminescence in the claims are not a technique. Please clarify.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 39-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Balazs (DE 3717212 A1, published on December 8, 1988).

Regarding claims 39 and 42, Balazs teaches a method for comparing an amount or concentration of total extracellular RNA or one or a plurality of RNA species thereof (ie., one of oncogenes in page 15 of English Translation of DE 3717212 A1) in blood plasma or serum or a

bodily fluid (ie., serum) from a human or animal with the amount or concentration of total extracellulr RNA or one or a plurality of RNA species thereon in blood plasma or serum or a bodily fluid (ie., serum) from a reference group or population (ie., other oncogenes in page 15 of English Translation of DE 3717212 A1), comprising the step of comparing the amount, concentration, signal intensity (ie., intensity of radioisotype on the X-ray film), color intensity, color, mass, or electrical property of total extracellular RNA or one or a plurality of RNA species thereof (see pages 12-19 in English Translation of DE 3717212 A1).

Regarding claims 40 and 43, Balazs teaches that the total extracellular RNA or one or a plurality of RNA species thereof from a human or animal is evaluated using hybridization (see pages 15 and 16 in English Translation of DE 3717212 A1).

Regarding claims 41 and 44, Balazs teaches that the total extracellular RNA or one or a plurality of RNA species thereof from a human or animal is evaluated using radioisotope-labeled probe or Northern blot analysis (see pages 15 and 16 in English Translation of DE 3717212 A1).

Therefore, Balazs teaches all limitations recited in claims 39-44.

14. Claims 42-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Datta *et al.,* (Journal of Clinical Oncology, 12, 475-482, 1994).

Regarding claim 42, Datta *et al.,* teach a method for comparing an amount or concentration of total extracellular RNA or one or a plurality of RNA species thereof (ie., K19 transcripts from patients with breast cancer) in a bodily fluid (ie., blood) from a human or animal with the amount or concentration of total extracellulr RNA or one or a plurality of RNA species

thereon in a bodily fluid (ie., blood) from a reference group or population (ie., K19 transcripts from patients without cancer), comprising the step of comparing the amount, concentration, signal intensity (ie., see gel bands in Figures 2-4), color intensity, color, mass, or electrical property of total extracellular RNA or one or a plurality of RNA species thereof (see abstract in page 475, 476, right column, Table 1 in page 477, and Figures 2-4).

Regarding claim 43, Datta *et al.,* teach that the total extracellular RNA or one or a plurality of RNA species thereof from a human or animal is evaluated using amplification (see 476, right column, Table 1 in page 477, and Figures 2-4).

Regarding claim 44, Datta *et al.,* teach that the total extracellular RNA or one or a plurality of RNA species thereof from a human or animal is evaluated using gel electrophoresis (see 476, right column, Table 1 in page 477, and Figures 2-4).

Therefore, Datta *et al.,* teach all limitations recited in claims 42-44.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 6,329,179 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims in this instant application is either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 in this instant application are not identical to claims 1-24 of U.S. Patent No. 6,329,179 B1, claims 1-24 of U.S. Patent No. 6,329,179 B1 are directed to the same subject matter and fall entirely within the scope of claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 in this instant application. In other words, claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 in this instant application are anticipated by claims 1-24 of U.S. Patent No. 6,329,179 B1.

17. Claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6,759,217 B2. Although the conflicting claims are not

identical, they are not patentably distinct from each other because the examined claims in this instant application is either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 in this instant application are not identical to claims 1-22 of U.S. Patent No. 6,759,217 B2, claims 1-22 of U.S. Patent No. 6,759,217 B2 are directed to the same subject matter and fall entirely within the scope of claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 in this instant application. In other words, claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 in this instant application are anticipated by claims 1-22 of U.S. Patent No. 6,759,217 B2.

18. Claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39 of U.S. Patent No. 6,916,634 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims in this instant application is either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 in this instant application are not identical to claims 1-39 of U.S. Patent No.

6,916,634 B2, 1-39 of U.S. Patent No. 6,916,634 B2 are directed to the same subject matter and fall entirely within the scope of claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 in this instant application. In other words, claims 1, 2, 4-6, 8, 9, 12-18, 20, 23-29, 31, 32, and 45-48 in this instant application are anticipated by claims 1-39 of U.S. Patent No. 6,916,634 B2.

Conclusion

19. No claim is allowed.

20. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

August 17, 2006

FRANK LU
PRIMARY EXAMINER